

REMARKS

After entry of this amendment, claims 34 to 63 will be pending. New claims 56 to 63 have been added. Support for the new claims is found in Example 1, Example 12 and Example 13.

The Office Action dated July 13, 2007 has been carefully reviewed and the following reply is made in response thereto. In view of the following remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Rejections under 35 U.S.C. § 103

The Examiner has rejected claims 34-42 and 45-55 under 35 U.S.C. § 103(a) as obvious under Latham *et al.* (J. of Virology 75, 6154-6165) in view of Saito *et al.* (Vaccine 20, 125-133). Specifically the Examiner asserts that he has made a *prima facie* of obviousness because:

The VLPs of Latham *et al.* react with monoclonal antibodies in western blots and on fixed cells and are stated by Latham *et al.* to be useful as vaccines. The VLPs are shown to look like influenza particles (Figure 5). The proteins that make the VLP of Latham *et al.* appear to be wild type in structure and antibody binding. The VLPs of Latham *et al.* would be expected to have the HA and NA activity of influenza. The claims recite no structures that differentiate them from the VLPs of Latham *et al.* (2/16/06).

Page 3, July 13, 2007 Office Action. In addition, the Examiner asserts that the HA and NA activity are properties of the recited structure, not structural features that exist on their own. *Id.*

1. Improper obviousness rejection

Applicants respectfully refer the Examiner to § 2112 of the MPEP which states that “[t]he fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic” (emphasis added). The Federal Circuit has consistently upheld this doctrine. Further, it is well settled that consideration of an inherent quality is generally relevant only to anticipation, not obviousness. *Jones v. Hardy*, 220 USPQ 1021, 1025 (Fed. Cir. 1984). Despite Applicants prior request to reconsider this issue, the Examiner has continued to use an inherency analysis for an obviousness rejection. Applicants

ask the Examiner to please point to case law that allows such an analysis. Respectfully, if the Examiner cannot point to case law allowing an inherency analysis for an obviousness rejection, then the rejections under 35 U.S.C. § 103 must be withdrawn.

2. The Examiner does not provide any evidence supporting his assertions of HA and/or NA activity in the cited art.

Assuming *arguendo* that the Examiner can point to case law that allows inherency analysis for an obviousness rejection, Applicants assert that the Examiner has not provided any evidenced to support his assertion that the HA and/or NA in Latham *et al.* inherently has activity. All the Examiner provides are assertions that the VLP of Latham *et al.* look like influenza particles, antibodies react to these proteins in western blots and fixed cells, the proteins that make the VLP of Latham *et al.* appear to be wild type in structure and antibody binding. By using these assertion, the Examiner assumes that the VLPs of Latham *et al.* “would be expected to have the HA and/or NA activity of influenza.”

“With regard to rejections under 35 U.S.C. 103, the examiner must provide evidence which as a whole shows that the legal determination sought to be proved (*i.e.*, the reference teachings establish a *prima facie* case of obviousness) is more probable than not.” MPEP 2142, emphasis added. In the instant case, the Examiner has not provided any evidence that HA and/or NA in Latham *et al.* has activity. The mere assertions, as listed above, are not enough. The Examiner must provide evidence of HA and/or NA activity in Latham *et al.* Thus, Applicants invite the Examiner to submit documentary evidence that HA and/or NA in Latham *et al.* have activity or the Examiner must take Official Notice without documentary evidence to support the his conclusion (see MPEP 2144.03). Otherwise, Applicants assert that the rejections under 35 U.S.C. § 103 must be withdrawn due to lack of evidence.

3. Scientific and legal analysis of the Examiner's assertions.

a. The Examiner has asserted that “[t]he VLPs of Latham *et al.* react with monoclonal antibodies in western blots and on fixed cells and are stated by Latham *et al.* to be useful as vaccines.” Applicants respectfully submit that just because “[t]he VLPs of Latham *et al.* react with monoclonal antibodies in western blots and on fixed cells and are stated by Latham *et al.* to

be useful as vaccines” does not imply that the HA and/or NA on the VLPs of Latham *et al.* have activity. There is no scientific basis to make such an assertion. Proteins on blots and proteins that are fixed generally do not have their natural conformation. Thus, there is no scientific rational to assume that just because antibodies react to a protein on a western blot or on fix cells that the protein in its natural state has activity. There are many examples in the art in which a protein has been mutated or denatured to abolish its activity which also bind to antibodies. One example is a toxoid. A toxoid, for example, reacts with antibodies in western blots, even though said toxoid, by definition, has no enzymatic activity.

b. Next, the Examiner asserts that “the HA and NA activity are properties of the recited structure, not structural features that exist on their own.” If by that statement the Examiner means that as long as the HA and/or NA is present, then said proteins will have activity, then Examiner is mistaken. There is absolutely no scientific basis to make such an assertion, nor has the Examiner pointed to any evidence that makes such an assertion possible. To express a protein that exhibits activity, the protein must be folded into the correct conformation. Expression and folding are complex processes that may not yield a protein with activity, especially in an *in-vivo* system. Thus, person of skill in the art would not assume that said proteins would have activity. In addition, the law does not allow for this assumption. “The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic.” MPEP § 2112, emphasis added. The Examiner has not conclusively shown, as required by the law, that HA and/or NA on the VLPs disclosed in Latham *et al.* have activity. Assertions and mere speculation are not enough.

c. Next, the Examiner asserts that “[t]he proteins that make the VLP of Latham *et al.* appear to be wild type in structure and antibody binding.” As stated above, “[t]he fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic.” *Id.*, emphasis added. Thus, just because proteins “appear to be wild type in structure and antibody binding,” does not guarantee that these proteins have activity. As stated above, there is absolutely no scientific basis to assume that just because antibodies react with their target protein that said protein has activity, nor is “appearing to be wild type in structure” a guarantee that said activity is present. The law states that the characteristic must be present. The Examiner has not established, by providing documents or by

taking Official Notice, that the HA and/or NA in Latham *et al.* have activity. Again, assertions and mere speculation are not enough. Thus, the burden is still on the Examiner to show that the HA and/or NA on the Latham *et al.* VLP have activity.

d. Next, the Examiner further asserts that “[t]he VLPs are shown to look like influenza particles (Figure 5).” Applicants interpret this statement this to mean that just because said VLPs disclosed in Latham *et al.* look like influenza particles, it would be expected that the proteins on the Latham *et al.* VLPs would possess activity.

Applicants traverse this reasoning. Again, Applicants point out that the Examiner does not cite to any references supporting this assertion. In addition, looking like an influenza particle does not guarantee that the HA and/or NA on the VLPs disclosed Latham *et al.* have activity. Applicants assert that a person of skill in the art cannot look at a picture of an influenza particle and assume that the HA and/or NA in the surface of said particle has activity. As stated above, “the fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic” (MPEP 2112, emphasis added). Thus, Applicants assert that the Examiner has not established a *prima facie* case of obviousness. In view of the above arguments, Applicants request that this rejection be reconsidered and withdrawn.

e. The Examiner has rejected claims 34, and 43-45 under 35 U.S.C. § 103(a) as being unpatentable over Latham *et al.* and Gupta *et al.* (Vaccine 3, 219-225). Specifically the Examiner asserts that Latham *et al.* discloses VLPs and Gupta *et al.* discloses Novasomes, thus rendering the claims obvious.

Applicants traverse this rejection and assert that the Examiner has not met his burden of establishing a *prima facie* case of obviousness. “To establish *prima facie* case of obviousness of a claimed invention, all claim limitation must be taught or suggested by the prior art” (MPEP 2143.03). As stated above, Latham *et al.* does not disclose avian influenza HA or NA proteins expressed on a VLP. In addition, Latham *et al.* does not show nor suggest that the HA or NA exhibit activity, as required by the claims (see above arguments). In addition, Gupta *et al.* does not disclose influenza vaccines in combination with adjuvants. Thus, the combined references do not teach or suggest all the claim elements. Therefore, the Examiner has not established a

prima facie case of obviousness. In view of the above argument, Applicants request that this rejection be reconsidered and withdrawn.

4. *Unexpected Results*

Applicants hereby submit a Declaration under 37 C.F.R. § 1.132 signed by Dr. Gale Smith which provides further evidence that the claimed invention is not obvious over the cited references. The Declaration describes experiments comparing VLP production between avian and seasonal influenza M1 proteins. The results of the experiments in the declaration indicate that avian M1 influenza protein, and not seasonal influenza M1 as used in Latham *et al.*, form VLPs efficiently either with homologous or heterologous envelope protein(s). These data also show the M1 from avian influenza is strongly expressed and stable when compared to seasonal influenza M1. Thus, Applicants have demonstrated the unexpected result that avian influenza M1 efficiently make VLPs when compared to non-avian (seasonal) influenza M1 protein. Such unexpected results are evidence of unobviousness. See *e.g.* MPEP 716.02(a) and the legal citations contained therein.

In summary, Applicants assert that the Examiner has mistakenly used an inherency analysis in an obviousness rejection and, assuming that the case law permits such an analysis (applicants have asked for such case law) that the Examiner has not met his burden of establishing a *prima facie* of obviousness. In addition, Applicants assert that the Declaration under 37 C.F.R. § 1.132 presents evidence of unexpected results, and thereby evidence of unobviousness.

Conclusion

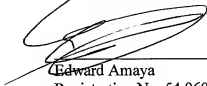
Applicant respectfully requests reconsideration of the subject application in view of the above remarks. It is respectfully submitted that this application is now in condition for allowance. Should the Examiner feel that there are any issues outstanding after consideration of this amendment; the Examiner is requested to contact the Applicant's undersigned representative.

If there are any fees due in connection with the filing of this amendment, please charge the fees to our Deposit Account No. **50-1283**. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

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